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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/237,291	01/25/1999	JUDY CAROL YOUNG	SYS-2068	9391
1095	7590	11/03/2005	EXAMINER	
NOVARTIS CORPORATE INTELLECTUAL PROPERTY ONE HEALTH PLAZA 104/3 EAST HANOVER, NJ 07936-1080			MONTANARI, DAVID A	
			ART UNIT	PAPER NUMBER
			1632	

DATE MAILED: 11/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/237,291	YOUNG ET AL.	
	Examiner	Art Unit	
	David Montanari	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 8/8/2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 18-20,23-27,31-34,37-43,46,47 and 52 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 18-20,23-27,31-34,37-43,46,47 and 52 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 08 March 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicants arguments and amendments filed on August 8th, 2005 have been entered.
2. Claims 48-51 are newly cancelled.
3. Rejection of claims 18, 23, 37, 43 under 35 USC 112, first paragraph is withdrawn.
4. Rejection of claims 18-20, 23-27, 31-34, 37-43, 46-47, and 52 under 35 USC 103(a) is withdrawn.
5. Claims 18-20, 23-27, 31-34, 37-43, 46-47, and 52 are examined in the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 18-20, 23-27, 31-34, 37-43, 46-47, and 52 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Dao et al. (01/15/1997, Blood, Vol. 89, pgs. 446-456) in view of Young et al. (09/01/1996, Blood, Vol. 88, pgs. 1619-1631).

Claims 18-20, 23-27, 31-34, 37-43, 46-47, and 52 are drawn to a method for obtaining genetically modified human pluripotent hematopoietic stem cells, comprising contacting a vector comprising a polynucleotide sequence encoding a heterologous gene with a population of human pluripotent hematopoietic stem cells cultured with fibronectin and in the presence of an effective amount of a mpl ligand and a flt3 ligand, each ligand provided in a concentration range of about 0.1 ng/mL to about 500 ng/mL, wherein said vector is selected from the group consisting of

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retroviral vectors, adenoviral vectors, and adeno-associated viral vectors and wherein said human pluripotent hematopoietic stem cells are $CD34^{+}$ $Thy-1^{+}$ Lin^{-} cells and can differentiate into any hematopoietic cell type; and obtaining said modified human pluripotent hematopoietic stem cells.

Dao et al. teach human $CD34^{+}$ progenitor cells transduced with retrovirus and cultured with FTL3 ligand (FL), to test whether FL might be able to replace the maintenance role provided by stromal support (pg. 446, Abstract). Dao continues to teach that said cells were cultured in the presence of interleukin-3 (IL-3), IL-6, and stem cell factor (SCF), and that the retrovirus contained the bacterial neomycin resistance gene (pg. 446 Abstract, and pg. 447, col. 2 parag. 4 lines 1-9). Dao obtained transduced $CD34^{+}$ cells and were examined with colony-forming assay (pg. 448, Fig. 1 and Table 1). Dao continues that “the combination of fibronectin, to enhance gene transfer, and FL, to support progenitor survival, may ultimately replace the use of patient-derived stromal layers” (pg. 455, col. 1 parag. 2).

Young et al. teach pluripotent $CD34^{+}$ $Thy-1$ Lin^{-} cells cultured with stromal support and thrombopoietin (TPO, an mpl ligand) and c-kit ligand (pg. 1620 col. 2 parag. 1). Young et al. continue to teach that TPO stimulated division of $CD34^{+}$ $Thy-1$ Lin^{-} cells, and further enhanced division when combined with IL-3 or c-kit ligand (pg. 1621 Fig. 1). Young continues that when TPO was combined with IL-3, cell production was enhanced 3-fold compared to TPO alone (pg. 1625, col. 1 lines 4-9). Young continues that “to transduce hematopoietic stem cells with exogenous gene using retroviral vectors, there is a requirement to induce cycling of quiescent cells without inducing differentiation. The effect we demonstrated here, that TPO activates PHP

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into cycle, has important implications for gene transduction into hematopoietic stem cells” (pg. 1630 col. 1 last parag. bridge col. 2 lines 1-2).

Thus the ordinary artisan would have been motivated at the time of filing to modify the method of Dao et al. in view of the teachings of Young et al. to use CD34⁺ Thy-1⁺ Lin⁻ cells to be transduced with a retrovirus vector and cultured with both a flt3 ligand and a mpl ligand with fibronectin given Dao teaching that FL in combination with fibronectin may eliminate the need for stromal support. Further motivation is provide by Young teaching that CD34⁺ Thy-1⁺ Lin⁻ cells cultured with TPO have enhanced cell production, and that TPO can aid in retrovirus-mediated transduction of hematopoietic stem cells. Thus the combined teachings of Dao and Young would both motivate and teach the ordinary artisan to make and use the claimed invention.

Applicant's arguments with respect to claim 18-20, 23-27, 31-34, 37-43, 46-47, and 52 have been considered but are moot in view of the new ground(s) of rejection.

No claims are allowed.

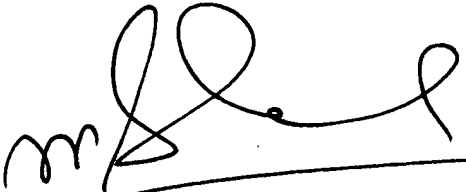
Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Montanari whose telephone number is 1-571-272-3108. The examiner can normally be reached on M-F 9-5:30.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 1-571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David A. Montanari, PhD


RAM R. SHUKLA, PH.D.
SUPERVISORY PATENT EXAMINER